



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2016-D-4318]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Guidance for Industry on Compounding and Repackaging of Radiopharmaceuticals by State-Licensed Nuclear Pharmacies, Federal Facilities, and Certain Other Entities

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Fax written comments on the collection of information by [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, Fax: 202-395-7285, or emailed to oir_submission@omb.eop.gov. All comments should be identified with the OMB control number 0910-NEW and title “Guidance for Industry on Compounding and Repackaging of Radiopharmaceuticals by State-Licensed Nuclear Pharmacies, Federal Facilities, and Certain Other Entities.” Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-5733, PRASStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Guidance for Industry on Compounding and Repackaging of Radiopharmaceuticals by State-Licensed Nuclear Pharmacies, Federal Facilities, and Certain Other Entities

OMB Control Number-NEW

This information collection supports the Agency guidance document entitled “Guidance for Industry on Compounding and Repackaging of Radiopharmaceuticals by State-Licensed Nuclear Pharmacies, Federal Facilities, and Certain Other Entities.”

Under current law, radiopharmaceuticals that are compounded by entities that are not registered with FDA as outsourcing facilities, and radiopharmaceuticals that are repackaged, are subject to all applicable provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act) related to drug production. Because Congress explicitly excluded radiopharmaceuticals from section 503A of the FD&C Act (21 U.S.C. 353a) (see section 503A(d)(2)), compounded radiopharmaceuticals are not eligible for the exemptions under section 503A from section 505 of the FD&C Act (21 U.S.C. 355) (concerning new drug approval requirements), section 502(f)(1) of the FD&C Act (21 U.S.C. 352(f)(1)) (concerning labeling with adequate directions for use), and section 501(a)(2)(B) of the FD&C Act (21 U.S.C. 351(a)(2)(B)) (concerning current good manufacturing practice requirements). In addition, the FD&C Act does not provide an exemption for repackaged radiopharmaceuticals.

FDA developed this guidance document to describe the conditions under which the Agency generally does not intend to take action for violations of sections 505, 502(f)(1), and 501(a)(2)(B) of the FD&C Act when a State-licensed nuclear pharmacy, Federal facility, or other facility that is not an outsourcing facility and that holds a radioactive materials license for medical use issued by the Nuclear Regulatory Commission or by an Agreement State compounds or repackages radiopharmaceuticals for human use.

One of the guidance document's conditions is that the compounded radiopharmaceutical is not essentially a copy of an approved radiopharmaceutical. If a compounder intends to rely on a determination from a prescriber that there is a change between the compounded radiopharmaceutical and the comparable approved radiopharmaceutical that produces a clinical difference for an identified individual patient, either the prescribing practitioner or the compounder documents the determination on the prescription or order in writing. This documentation reflects a conversation with the prescribing practitioner, and the compounder maintains records of the prescription or order documenting this determination.

In the *Federal Register* of December 29, 2016 (81 FR 96011), FDA published a notice of availability for the draft guidance, including a 60-day notice soliciting public comment on the information collection recommendations. Several comments were received and are discussed below; however, none of the comments suggested we revise the burden estimate from our 60-day notice.

(Comment 1) One commenter said documentation of a minor deviation from an approved radiopharmaceutical should remain at the facility that performed the minor deviation.

(Response 1) The documentation condition (i.e., documentation of a prescriber's determination that there is a change that produces a clinical difference between the compounded

radiopharmaceutical and the comparable FDA-approved radiopharmaceutical for an identified individual patient) does not apply to compounding that consists only of minor deviations as defined in the guidance document (i.e., a change from the approved labeling in radioactivity, volume, or the step-by-step procedures made when compounding the radiopharmaceutical from an FDA-approved drug product in a patient-ready dose). The documentation condition applies to compounding a radiopharmaceutical that involves manipulation other than minor deviations.

(Comment 2) One commenter supports the requirement for notating clinical differences, particularly for documenting both the change to the radiopharmaceutical and the reason that the change is important for the patient.

(Response 2) FDA concurs with this commenter's views about the importance of the documentation. FDA's guidance document states that the documentation condition would be met if the prescription for the compounded radiopharmaceutical makes clear that the prescriber identified the relevant change between the approved radiopharmaceutical and the compounded radiopharmaceutical and the clinical difference that the change produces for the patient.

(Comment 3) One commenter recommended that the guidance document require written documentation when a commercially manufactured radiopharmaceutical is compounded for a patient because the radiopharmaceutical is unavailable due to a drug shortage.

(Response 3) The guidance document explains that FDA does not consider a compounded radiopharmaceutical to be essentially a copy of a marketed FDA-approved radiopharmaceutical if the FDA-approved radiopharmaceutical is on FDA's drug shortage list (see section 506E of the FD&C Act (21 U.S.C. 356e)) at the time of compounding and distribution. FDA maintains a database for drug shortages. If the Agency identifies a compounded radiopharmaceutical that has the characteristics of a drug that is "essentially a

copy,” FDA intends to review its database to determine whether there was a shortage of the approved radiopharmaceutical at the time of compounding and distribution.

FDA estimates the burden of this collection of information as follows:

Table 1.--Estimated Annual Third-Party Disclosure Burden¹

Type of Reporting	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
Consultation between the compounder and prescriber and the notation on the prescription or order documenting the prescriber's determination of clinical difference	10	25	250	0.05 (3 minutes)	12.5

¹There are no capital costs or operating and maintenance costs associated with this collection of information.

The total estimated third-party disclosure burden for the guidance document is shown above.

We estimate that a total of approximately 10 compounders annually (“No. of Respondents” in table 1, line 1) will consult a prescriber to determine whether they decided that the compounded radiopharmaceutical has a change that produces a clinical difference for an identified individual patient as compared to the comparable approved radiopharmaceutical. We estimate that compounders will document this determination on approximately 250 prescriptions or orders for compounded radiopharmaceuticals (“Total Annual Disclosures” in table 1, line 1). We estimate that the consultation between the compounder and the prescriber and noting this determination on each prescription or order that does not already document this determination will take approximately 3 minutes per prescription or order.

In the *Federal Register* of December 29, 2016 (81 FR 96011), FDA also estimated the annual recordkeeping burden for maintaining records of prescriptions or orders documenting certain information from prescribers. While acquiring additional information from the public about State pharmacy practices since we published 81 FR 96011, FDA has determined that

because the time, effort, and financial resources necessary to comply with this collection of information would be incurred by compounders in the normal course of their activities, it is excluded from the definition of “burden” under 5 CFR 1320.3(b)(2). FDA understands that maintaining records of prescriptions for compounded drug products is part of the usual course of the practice of compounding and selling drugs and is required by States’ pharmacy laws and other State laws governing record keeping by healthcare professionals and healthcare facilities.

Dated: July 10, 2018.

Leslie Kux,

Associate Commissioner for Policy.

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